



M10988. Reports Human tumor necro...[gi:339737]

Links

LOCUS HUMTNFAA 1585 bp mRNA linear PRI 14-JAN-1995
DEFINITION Human tumor necrosis factor (TNF) mRNA.
ACCESSION M10988
VERSION M10988.1 GI:339737
KEYWORDS .
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 1585)
AUTHORS Wang, A. M., Creasey, A. A., Ladner, M. B., Lin, L. S., Strickler, J., Van
Arsdell, J. N., Yamamoto, R. and Mark, D. F.
TITLE Molecular cloning of the complementary DNA for human tumor necrosis
factor
JOURNAL Science 228 (4696), 149-154 (1985)
MEDLINE 85142190
PUBMED 3856324

COMMENT Original source text: Human cDNA to mRNA, clone pE4.

FEATURES Location/Qualifiers

source 1..1585
/organism="Homo sapiens"
/mol_type="mRNA"
/db_xref="taxon:9606"
/map="6p21.3"

gene 1..1585
/gene="TNFA"

CDS 86..787
/gene="TNFA"
/note="tumor necrosis factor"
/codon_start=1
/protein_id="AAA61198.1"
/db_xref="GI:339738"
/db_xref="GDB:G00-120-441"
/translation="MSTESMIRDVELAEEALPKKTGGPQGSRRCLFLSFLIVAGA
TTLFCLLHFGVIGPQREESPRDLSLISPLAQAVRSSSRTPSDKPVAVHVVANPQAEQQL
QWLNRRANALLANGVELRDNLVVPSEGLYLYSQVLFKGQGPCSTHVLLTHTISRIA
VSYQTKVNLLSAIKSPCQRETPEGAEAKPWYEPILGGVFQLEKGDRLSAEINRPDYL
DFAESGQVYFGIIAL"

ORIGIN Chromosome 6p21.3.

1 cacaccctga caagctgcc a ggcaggttct cttcctctca catactgacc cacggctcca
61 cctctctctcc cctggaaagg acaccatgag cactgaaagc atgatccggg acgtggagct
121 ggccgaggag gcgctcccca agaagacagg ggggccccag ggctccaggc ggtgcttgtt
181 cctcagcctc ttctccttcc tgatcgtggc aggcgccacc acgctcttct gcctgctgca

241 ctttggagtg atcgggcccc agaggggaaga gtcccccagg gacctctctc taatcagccc
301 tctggcccag gcagtcagat catcttctcg aaccccagtg gacaagcctg tagcccatgt
361 tgtagcaaac cctcaagctg aggggcagct ccagtggctg aaccgccggg ccaatgccct
421 cctggccaat ggcgtaggagc tgagagataa ccagctgggtg gtgccatcag agggcctgta
481 cctcatctac tcccagggtcc tcttcaaggg ccaaggctgc ccctccaccc atgtgctcct
541 caccacacacc atcagccgca tcgccgtctc ctaccagacc aaggtcaacc tcctctctgc
601 catcaagagc ccctgccaga gggagacccc agagggggct gaggccaagc cctggtatga
661 gcccatctat ctgggagggg tcttccagct ggagaagggt gaccgactca gcgctgagat
721 caatcgggcc gactatctcg actttgccga gtctgggcag gtctactttg ggatcattgc
781 cctgtgagga ggacgaacat ccaaccttc caaacgcctc ccctgcccc atccctttat
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901 ggtcggaacc caagcttaga actttaagca acaagaccac cacttcgaaa cctgggattc
961 aggaatgtgt ggccctgcaca gtgaagtgt ggcaaccact aagaattcaa actggggcct
1021 ccagaactca ctggggccta cagctttgat ccctgacatc tggaatctgg agaccaggga
1081 gcctttggtt ctggccagaa tgctgcagga cttgagaaga cctcacctag aaattgacac
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1201 cagccctccc catggagcca gctccctcta tttatgtttg cacttgtgat tatttattat
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1441 aaaatattat ctgattaagt tgtctaaaca atgctgattt ggtgaccaac tgtcactcat
1501 tgctgaggcc tctgctcccc agggagtgt gtctgtaatc ggcctactat tcagtggcga
1561 gaaataaagg ttgcttagga aagaa

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BLink,
Domains,
Links

1: Q8HZD9. Reports Tumor necrosis fa...[gi:31077029]

LOCUS Q8HZD9 232 aa linear PRI 15-JUN-2004

DEFINITION Tumor necrosis factor precursor (TNF-alpha) (Tumor necrosis factor ligand superfamily member 2) (TNF-a) (Cachectin).

ACCESSION Q8HZD9

VERSION Q8HZD9 GI:31077029

DBSOURCE swissprot: locus TNFA_PANTR, accession Q8HZD9;
class: standard.
created: Oct 10, 2003.
sequence updated: Oct 10, 2003.
annotation updated: Jun 15, 2004.
xrefs: gi: [18181946](#), gi: [18181948](#), gi: [32127763](#), gi: [32127765](#), gi: [23379678](#), gi: [23379679](#)
xrefs (non-sequence databases): HSSPP01375, InterProIPR006053, InterProIPR006052, InterProIPR008983, InterProIPR003636, PfamPF00229, PRINTSPR01234, ProDomPD002012, PROSITEPS00251, PROSITEPS50049

KEYWORDS Cytokine; Transmembrane; Signal-anchor; Phosphorylation.

SOURCE Pan troglodytes (chimpanzee)

ORGANISM Pan troglodytes
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Pan.

REFERENCE 1 (residues 1 to 232)

AUTHORS Kulski, J.K., Shiina, T., Anzai, T., Kohara, S. and Inoko, H.

TITLE Comparative genomic analysis of the MHC: the evolution of class I duplication blocks, diversity and complexity from shark to man

JOURNAL Immunol. Rev. 190, 95-122 (2002)

MEDLINE [22381002](#)

PUBMED [12493009](#)

REMARK SEQUENCE FROM N. A.

REFERENCE 2 (residues 1 to 232)

AUTHORS Anzai, T., Shiina, T., Kimura, N., Yanagiya, K., Kohara, S., Shigenari, A., Yamagata, T., Kulski, J.K., Naruse, T.K., Fujimori, Y., Fukuzumi, Y., Yamazaki, M., Tashiro, H., Iwamoto, C., Umehara, Y., Imanishi, T., Meyer, A., Ikeo, K., Gojobori, T., Bahram, S. and Inoko, H.

TITLE Comparative sequencing of human and chimpanzee MHC class I regions unveils insertions/deletions as the major path to genomic divergence

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 100 (13), 7708-7713 (2003)

MEDLINE [22709134](#)

PUBMED [12799463](#)

REMARK SEQUENCE FROM N. A.

REFERENCE 3 (residues 1 to 232)
 AUTHORS O'Huigin, C., Tichy, H. and Klein, J.
 TITLE Direct Submission
 JOURNAL Submitted (??-MAR-2002)
 REMARK SEQUENCE OF 33-186 FROM N. A.

COMMENT

 This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation - the European Bioinformatics Institute. The original entry is available from <http://www.expasy.ch/sprot> and <http://www.ebi.ac.uk/sprot>

[FUNCTION] Cytokine that binds to TNFRSF1A/TNFR1 and TNFRSF1B/TNFR. It is mainly secreted by macrophages and can induce cell death of certain tumor cell lines. It is potent pyrogen causing fever by direct action or by stimulation of interleukin 1 secretion and is implicated in the induction of cachexia, Under certain conditions it can stimulate cell proliferation and induce cell differentiation (By similarity).

[SUBUNIT] Homotrimer (By similarity).

[SUBCELLULAR LOCATION] Type II membrane protein. Also exists as an extracellular soluble form (By similarity).

[PTM] The soluble form derives from the membrane form by proteolytic processing (By similarity).

[PTM] The membrane form, but not the soluble form, is phosphorylated on serine residues. Dephosphorylation of the membrane form occurs by binding to soluble TNFRSF1A/TNFR1 (By similarity).

[SIMILARITY] Belongs to the tumor necrosis factor family.

FEATURES

	Location/Qualifiers
source	1..232 /organism="Pan troglodytes" /db_xref="taxon:9598"
<u>gene</u>	1..232 /gene="TNF" /note="synonyms: TNFSF2, TNFA"
<u>Protein</u>	1..232 /gene="TNF" /product="Tumor necrosis factor precursor"
<u>Region</u>	1..232 /gene="TNF" /region_name="Mature chain" /note="Tumor necrosis factor, membrane form (By similarity)."

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/evidence=experimental
Region 1..34
/gene="TNF"
/region_name="Domain"
/note="Cytoplasmic (Potential)."
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Site 2

```

/evidence=experimental
/gene="TNF"
/site_type="modified"
/note="Phosphoserine (by CK1) (By similarity)."
```

Region 35..57

```

/evidence=experimental
/gene="TNF"
/region_name="Transmembrane region"
/note="Signal-anchor for type II membrane protein (By
similarity)."
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Region 58..232

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/evidence=experimental
/gene="TNF"
/region_name="Domain"
/note="Extracellular (Potential)."
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Site 76..77

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/evidence=experimental
/gene="TNF"
/site_type="cleavage"
/note="Cleavage (by ADAM17) (By similarity)."
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Region 77..232

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/evidence=experimental
/gene="TNF"
/region_name="Mature chain"
/note="Tumor necrosis factor, soluble form (By
similarity)."
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Region 77

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/evidence=experimental
/gene="TNF"
/region_name="Conflict"
/note="G -> VR (in Ref. 3)."
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Bond bond(144,176)

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/evidence=experimental
/gene="TNF"
/bond_type="disulfide"
/note="By similarity."
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ORIGIN

1 mstesmirdv elaealpkk tggpqgsrrc lfslfsfli vagattlfcl lhfgvigpqr
61 eefprdlsl i splaqagsss rtpsdkpvh vvanpqaegq lqwnrrana llangvelrd
121 nqlvpsegl yliysqvlfk gqgcpsthv lthtisriav syqtkvnlls aikspcqret
181 pegaeakpwy epiylggvfq lekgdrisae inrpdylfa esgvyfgii al

1: X02910. Reports Human gene for tu...[gi:37209] Links

LOCUS HSTNFA 3634 bp DNA linear PRI 17-FEB-1997

DEFINITION Human gene for tumor necrosis factor (TNF-alpha).

ACCESSION X02910 X02159

VERSION X02910.1 GI:37209

KEYWORDS signal peptide; tumor necrosis factor.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1

AUTHORS Pennica, D., Nedwin, G. E., Hayflick, J. S., Seeburg, P. H., Derynck, R.,
Palladino, M. A., Kohr, W. J., Aggarwal, B. B. and Goeddel, D. V.

TITLE Human tumour necrosis factor: precursor structure, expression and
homology to lymphotoxin

JOURNAL Nature 312 (5996), 724-729 (1984)

MEDLINE 85086244

PUBMED 6392892

REFERENCE 2 (bases 329 to 3634)

AUTHORS Shirai, T., Yamaguchi, H., Ito, H., Todd, C. W. and Wallace, R. B.

TITLE Cloning and expression in Escherichia coli of the gene for human
tumour necrosis factor

JOURNAL Nature 313 (6005), 803-806 (1985)

MEDLINE 85137898

PUBMED 3883195

REFERENCE 3 (bases 1 to 3634)

AUTHORS Nedwin, G. E., Naylor, S. L., Sakaguchi, A. Y., Smith, D.,
Jarrett-Nedwin, J., Pennica, D., Goeddel, D. V. and Gray, P. W.

TITLE Human lymphotoxin and tumor necrosis factor genes: structure,
homology and chromosomal localization

JOURNAL Nucleic Acids Res. 13 (17), 6361-6373 (1985)

MEDLINE 86016093

PUBMED 2995927

COMMENT In the cDNA sequence from ref [3] the mature protein site starts
also with Val at pos 1631
Data kindly reviewed (18-FEB-1986) by A. Sakaguchi.

FEATURES Location/Qualifiers

source 1..3634
/organism="Homo sapiens"
/mol_type="genomic DNA"
/db_xref="taxon:9606"

TATA signal 590..595

prim transcript 615..3381
/note="put. primary transcript"

exon 615..981
 /number=1
conflict 768
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 /translation="MSTESMIRDVELAEEALPKKTGGPQGSRRCLFLSLFSFLIVAGA
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 QWLNRRANALLANGVELRDNLVVPSEGLYLIYSQVLFKGGQCPSTHVLLTHTISRIA
 VSYQTKVNLLSAIKSPCQRETPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYL
 DFAESGQVYFGIIAL"
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 ref. [2])"
mat_peptide join(1631..1634, 1822..1869, 2171..2589)
 /product="TNF-alpha"
intron 982..1588
 /number=1
conflict 1092
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 /citation=[2]
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exon 1589..1634
 /number=2
intron 1635..1821
 /number=2
exon 1822..1869
 /number=3
misc_feature 1822..1823
 /note="put. signal peptide (aa -1, ref. [2])"
misc_feature 1824..1869
 /note="TNF-alpha (aa 1-15, ref. 2)"
intron 1870..2170
 /number=3
exon 2171..3381
 /number=4
misc_feature 2171..2589
 /note="TNF-alpha (aa 18-157; aa 16-155 in ref. [2])"

conflict 2791
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/replace="t"
conflict 2882
/citation=[2]
/replace="a"
conflict 3326
/citation=[2]
/replace="a"
polyA signal 3368..3373
polyA site 3381

ORIGIN

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121 caggcctcag gactcaacac agcttttccc tccaaccgt tttctctccc tcaacggact
181 cagctttctg aagcccctcc cagtcttagt tctatctttt tctgcatcc tgtctggaag
241 ttagaaggaa acagaccaca gacctggtcc ccaaagaaa tggaggcaat aggttttgag
301 gggcatgggg acgggggttca gcctccaggg tctacacac aaatcagtca gtggcccaga
361 agacccccct cggaatcgga gcaggaggga tggggagtgt gaggggtatc cttgatgctt
421 gtgtgtcccc aactttccaa atccccgcc ccgcgatgga gaagaaaccg agacagaagg
481 tgcaggggccc actaccgctt cctccagatg agctcatggg tttctccacc aaggaagttt
541 tccgctgggt gaattattct ttccccgcc tcctctcgcc ccagggacat ataaaggcag
601 ttgttgccac acccagccag cagacgtcc ctcagcaagg acagcagagg accagctaag
661 agggagagaa gcaactacag accccccctg aaaacaaccc tcagacgcca catccctga
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1801 tcttttctct ctcctcttca ggatcatctt ctcgaacccc gagtgaacaag cctgtagccc
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1921 ttgaagcccg gctgatggta ggcagaactt ggagacaatg tgagaaggac tcgctgagct
1981 caagggaagg gtggaggaac agcacaggcc ttagtgggat actcagaacg tcatggccag
2041 gtgggatgtg ggatgacaga cagagaggac aggaaccgga tgtggggtgg gcagagctcg
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3601 ctgaggcat gggaatttcc aactctggga attc

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Molecular cloning of the complementary DNA for human tumor necrosis factor.

Wang AM, Creasey AA, Ladner MB, Lin LS, Strickler J, Van Arsdel JN, Yamamoto R, Mark DF.

Tumor necrosis factor (TNF) is a soluble protein that causes damage to tumor cells but has no effect on normal cells. Human TNF was purified to apparent homogeneity as a 17.3-kilodalton protein from HL-60 leukemia cells and showed cytotoxic and cytostatic activities against various human tumor cell lines. The amino acid sequence was determined for the amino terminal end of the purified protein, and oligodeoxyribonucleotide probes were synthesized on the basis of this sequence. Complementary DNA (cDNA) encoding human TNF was cloned from induced HL-60 messenger RNA and was confirmed by hybrid-selection assay, direct expression in COS-7 cells, and nucleotide sequence analysis. The human TNF cDNA is 1585 base pairs in length and encodes a protein of 233 amino acids. The mature protein begins at residue 77, leaving a long leader sequence of 76 amino acids. Expression of high levels of human TNF in *Escherichia coli* was accomplished under control of the bacteriophage lambda PL promoter and gene N ribosome binding site.